

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
18 July 2002 (18.07.2002)

PCT

(10) International Publication Number  
**WO 02/054872 A1**

(51) International Patent Classification<sup>7</sup>: **A01N 59/24**, 59/12, A61L 2/18, A61K 33/40, 33/18 // (A01N 59/24, 59:12)

David, Wilson [GB/GB]; 5 Morley's Close, Lowdham, Nottinghamshire NG14 7HN (GB).

(21) International Application Number: PCT/GB02/00025

(74) Agents: LYONS, June, M. et al.; Mewburn Ellis, York House, 23 Kingsway, London, Greater London WC2B 6HP (GB).

(22) International Filing Date: 4 January 2002 (04.01.2002)

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

(25) Filing Language: English

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(26) Publication Language: English

Published:

— with international search report

(30) Priority Data:  
0100643.6 10 January 2001 (10.01.2001) GB

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(71) Applicant (for all designated States except US): BASF AKTIENGESELLSCHAFT [DE/DE]; Ludwigshafen, D-67056 Germany (DE).

(72) Inventors; and

(75) Inventors/Applicants (for US only): GUTHRIE, Walter, Graham [GB/GB]; 7 Rope Walk, East Leake, Loughborough, Leicestershire LE12 6NR (GB). QURESH, Mohammed, Shoaib [GB/GB]; 4 Maple Close, Bingham, Nottinghamshire NG13 8GY (GB). STANIFORTH, Lawrence, Alan [GB/GB]; 14 Lichfield Road, Sneinton, Nottinghamshire NG2 4GG (GB). HODGKINSON, Darren, Michael [GB/GB]; 41 Bentinck Street, Hucknall, Nottinghamshire NG15 7GH (GB). ASHWORTH,



WO 02/054872 A1

(54) Title: LIQUID ANTIMICROBIAL COMPOSITIONS

(57) Abstract: ABSTRACT LIQUID ANTIMICROBIAL COMPOSITIONS A liquid antimicrobial composition comprises:(1) a mixture of iodide anions and thiocyanate anions;(2) periodic acid or an alkali metal salt thereof; and(3) optionally, a peroxidase. The composition may be used as a microbicide, disinfectant or for suppressing or killing viruses or spores.

Liquid Antimicrobial Compositions

This invention relates to an antimicrobial composition comprising iodide and thiocyanate anions.

5

Particular compositions of this type are disclosed in WO-A-91/11105. These compositions comprise

- (1) iodide and thiocyanate anions in a weight:weight ( $I^-:SCN^-$ ) ratio of 0.1:1 to 50:1 and in a combined anion weight concentration of at least 5mg/kg;
- 10 (2) D-glucose in a weight concentration of at least 0.2g/kg;
- (3) glucose oxidase as an oxidoreductase enzyme; and
- (4) optionally, a peroxidase, especially

15 lactoperoxidase.

Preferred such compositions of WO-A-91/11105 are preservative compositions in a solid (dry powder), or liquid two-pack, form in which one pack contains the D-glucose and the other the glucose oxidase. The contents of the two packs are mixed and immediately used.

On the other hand WO-A-95/26137 describes antimicrobial compositions containing the same components as those of WO-A-91/11105 and preferably in the same proportions. However, WO-A-95/26137 does not recommend the immediate use of components mixed together; rather, it teaches the provision of an incubation period of from 12 - 48 hours before use. From this, it is clear that in order to 25 achieve an antimicrobial effect using such compositions, it is necessary to allow the components to react with one

another to form a reaction product which then has the desired rapid antimicrobial activity.

As an alternative to compositions containing iodide and 5 thiocyanate anions, antimicrobial compositions are known which are based on periodic acid, which is a known oxidising agent and electron acceptor. For example, DE-A-4301277 describes the use of periodic and/or orthoperiodic acid for the sterilisation of containers 10 for storage and transportation of milk by treating the internal surfaces of the container at room temperature for 2 - 20 seconds with an aqueous solution of 0.1 to 5 wt% of periodic or orthoperiodic acid.

15 EP-A-0726357 describes a process for inhibiting the production and accumulation of volatile fatty acids by hydrolytic fermentative bacteria in an anionic pulp and paper processing stream in which the presence of hydrogen is monitored and at least one of a biocide and an 20 electron acceptor is added. The use of sodium (para) periodate is recommended for the case where the presence of an electron acceptor and some inhibition of the microorganisms is required.

25 We have now found surprisingly that if, in an antimicrobial composition containing iodide and thiocyanate ions, D-glucose and glucose oxidase (such as a composition described in WO-A-91/11105 or WO-A-95/26137), the D-glucose and glucose oxidase in 30 combination are replaced solely by periodic acid or an alkali metal salt thereof, an efficient liquid antimicrobial composition is obtained, which is capable

of having a rapid killing effect upon the microorganisms which it is used to treat.

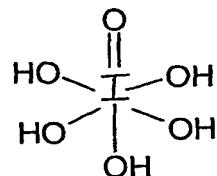
Thus, according to one aspect, the invention provides a  
5 liquid antimicrobial composition comprising

(1) a mixture of iodide anions and thiocyanate anions;

(2) periodic acid or an alkali metal salt thereof;  
and

10 (3) optionally, a peroxidase.

Periodic acid [CAS RN 10450-60-9], sometimes referred to as an orthoperiodic acid, has the formula



15 Preferably, the periodic acid or salt thereof is present in the composition in an amount of from 25 to 500 ppm, more preferably from 200 to 500 ppm, by weight of the total weight of the composition.

20 Thus, even a composition containing as low an amount of periodic acid as 25 - 50 ppm can kill bacteria such as E.coli but for a broad spectrum of activity, the minimum amount should be about 100 ppm. Moreover, for a stable shelf life, at least 200 ppm is preferred. The preferred  
25 maximum amount is about 500 ppm.

Such compositions react considerably faster than the composition disclosed in WO-A-91/11105 and WO-A-95/26137

so that, instead of the 4 - 48 hours recommended for optimum potency, compositions embodying the invention may achieve a rapid kill of microorganisms immediately after mixing.

5

In contrast to the two-pack forms disclosed in WO-A-91/11105 and WO-A-95/26137 for use as a preservative, a liquid composition embodying the invention can be used as a disinfectant, in the form of a single, ready to use, 10 product.

15 The spectrum of antimicrobial activity is also somewhat different from that of the abovementioned known compositions. In particular, compositions embodying the invention are particularly effective in combatting viruses and spores, e.g. bacillus spores.

20 The precise role played by the periodic acid in improving the antimicrobial efficiency of the iodide/thiocyanate anion system is not fully understood, although the mechanism seems to involve oxidation.

25 The pH of the composition may be from, say, 1 to 8 but is preferably less than 4.5 and, especially at low pH, the composition may contain free periodic acid. However, the composition may alternatively or additionally contain an alkali metal, especially the sodium, salt thereof.

30 As indicated above, the composition may additionally contain a peroxidase, especially lactoperoxidase; the presence of a peroxidase is surprisingly found to improve the shelf life of the composition. Thus, although this

might have been expected for an organic oxidation/reduction system as in WO-A-91/11105, it is surprising that such an effect is achievable with an inorganic system utilizing periodic acid.

5

Preferably the peroxidase is present in the composition in an amount of at least 10 U/kg.

10 In a composition embodying the invention, the weight:weight ratio of iodide:thiocyanate anions is preferably from 0.1:1 to 50:1, more preferably from 0.2:1 to 20:1 inclusive.

15 The iodide and thiocyanate anions are preferably present in the composition in a total amount of at least 5 mg/kg, based on the total weight of the composition. The iodide anions are preferably present in the composition at a weight concentration of at least 5 mg/kg, while the thiocyanate ions are preferably present at a weight 20 concentration of at least 2 mg/kg, based on the total weight of the composition.

25 A composition embodying the invention may contain additionally a suitable carrier. Preferably, the carrier is water and the composition is an aqueous solution. However, the carrier may comprise water and, additionally, a surfactant or emulsifier, whereby the composition is an oil in water emulsifier or a surfactant based solution.

30

According to other aspects, the invention provides the use of a composition as defined above as a microbicide or

as a disinfectant respectively and especially the use of such a composition for suppressing or killing viruses or spores, e.g. bacillus spores.

5 In addition to the use of the composition as a microbicide or disinfectant, an anti-microbial composition embodying the invention may provide the active component in a wide variety of products which require potent antibacterial, anti-mould and/or anti-10 yeast activities. Examples of such products include:

a) deodorants e.g. for topical administration in the form of lotions;

15 b) antibacterial skin washes e.g. in the forms of lotions;

c) anti-acne preparations e.g. in the form of lotions or creams;

20 d) anti-athletes foot preparations e.g. in the form of lotions;

e) anti-dandruff preparations e.g. in the form of 25 shampoos or lotions;

f) dental preparations, e.g. mouth washes suitable for general oral hygiene and, in particular, having anti-plaque properties, and dentrifices such as toothpastes, 30 chewing gums and lozenges;

- g) impregnated materials e.g. wound dressings, sutures and dental floss;
- h) pharmaceuticals e.g. wound irrigants and burn treatments, anti-diarrhoeal agents and medicaments suitable for the treatment of infections such as Candida and Tinea infections;
- i) ophthalmic preparations e.g. eye washes and/or sterilising contact lenses; and
- j) sterilants e.g. for baby bottles and surgical or dental instruments.

15 According to yet another aspect, the invention provides a method of killing or suppressing viruses or spores comprising contacting them within a composition as defined above.

20 Embodiments of the invention will now be described in more detail with reference to the following Examples.

Example

25 A composition contains

- 1. NaSCN 4.2 mg
- 2. KI 7.3 mg
- 3. Lactoperoxidase 70 international units
- 30 4. Periodic acid 200 mg
- 5. Water up to 100 ml.

Components 1 - 4 were added to 75 mls of distilled water and stirred until dissolved. The solution was then made up to 100 mls with distilled water.

5 The above solution was then immediately challenged with a  $1 \times 10^6$  cfu/ml inoculum of the following organisms.

Ps.aeruginosa NCIB 8626

S.aureus NCIB 9518

10 E.coli NCIB 8545

C.albicans ATCC 1023

A. niger ATCC 16404

15 Total kill of each of the above organisms was achieved in less than 5 mins.

Excellent anti-viral activity was also demonstrated against Echovirus 11 and Herpes simplex virus type 1 (HSV-1).

20

Excellent sporicidal activity was also demonstrated against B.cereus NCTC 2599 and B.subtilis NCTC 10073.

25

The solution was still demonstrating the above activity after six months storage at room temperature.

Claims

1. A liquid antimicrobial composition comprising:
  - (1) a mixture of iodide anions and thiocyanate anions;
  - (2) periodic acid or an alkali metal salt thereof; and
  - (3) optionally, a peroxidase.
- 5 10 2. A composition according to claim 1, wherein the periodic acid or salt thereof is present in the composition in an amount of from 25 to 500 ppm by weight of the total weight of the composition.
- 15 3. A composition according to claim 2, wherein the periodic acid or salt thereof is present in an amount of from 200 to 500 ppm by weight of the total weight of the composition.
- 20 4. A composition according to any preceding claim, wherein the weight:weight ratio of iodide:thiocyanate anions is from 0.1:1 to 50:1 inclusive.
- 25 5. A composition according to claim 4, wherein the weight:weight ratio of iodide:thiocyanate anions is from 0.2:1 to 20:1 inclusive.
- 30 6. A composition according to any preceding claim, wherein the iodide and thiocyanate anions are present in the composition in a total weight of at least 5 mg/kg, based on the total weight of the composition.

7. A composition according to any preceding claim, wherein the iodide anions are present in the composition to a weight concentration of at least 5 mg/kg and the thiocyanate ions to a weight concentration of at least 2 mg/kg, based on the total weight of the composition.

8. A composition according to any preceding claim, which contains a peroxidase.

10 9. A composition according to claim 8, wherein the peroxidase is lactoperoxidase.

10 10. A composition according to claim 8 or claim 9, wherein the peroxidase is present in the composition in 15 an amount of at least 10 U/kg.

11. A composition according to any preceding claim which additionally contains a suitable carrier.

20 12. A composition according to claim 11, wherein the carrier is water and the composition is an aqueous solution.

25 13. A composition according to claim 12, wherein the carrier additionally comprises a surfactant or emulsifier and the composition is an oil in water emulsifier or a surfactant based solution.

30 14. Use of a composition according to any preceding claim as a microbicide.

15. Use of a composition according to any one of claims 1 to 13 as a disinfectant.

16. Use of a composition according to any one of claim 1 to 14 for suppressing or killing viruses or spores.

17. A method of killing or suppressing viruses or spores comprising contacting them with a composition according to any one of claims 1 to 13.

# INTERNATIONAL SEARCH REPORT

Inte  
rnal Application No  
PCT/GB 02/00025

**A. CLASSIFICATION OF SUBJECT MATTER**  
 IPC 7 A01N59/24 A01N59/12 A61L2/18 A61K33/40 A61K33/18  
 // (A01N59/24, 59:12)

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
 IPC 7 A01N A61L A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

| Category | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No. |
|----------|---|-----------------------|
| A        | WO 95 26137 A (BOOTS CO PLC ; ASHWORTH DAVID WILSON (GB); GUTHRIE WALTER GRAHAM (G) 5 October 1995 (1995-10-05)<br>cited in the application<br>page 1, line 6-21<br>page 4, line 8 -page 5, line 10 | 1-17                  |
| A        | WO 91 11105 A (BOOTS CO PLC)<br>8 August 1991 (1991-08-08)<br>cited in the application<br>page 1, line 10 -page 2, line 24<br>page 5, line 31 -page 6, line 27<br>page 6, line 28 -page 7, line 20  | 1-17                  |
| A        | DE 43 01 277 A (STUBINITZKY HEINZ GUENTER)<br>14 July 1994 (1994-07-14)<br>cited in the application<br>column 1, line 50-55; claims 1,5   | 1-17                  |

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

\* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority, claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

22 March 2002

02/04/2002

Name and mailing address of the ISA  
 European Patent Office, P.B. 5818 Palentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
 Fax: (+31-70) 340-3016

Authorized officer

Klaver, J

# INTERNATIONAL SEARCH REPORT

Information on patent family members

Int'l  
nal Application No  
PCT/GB 02/00025

| Patent document cited in search report | Publication date | Patent family member(s) |             | Publication date |
|--|------------------|-------------------------|-------------|------------------|
| WO 9526137                             | A 05-10-1995     | AU                      | 697046 B2   | 24-09-1998       |
|  |                  | AU                      | 2110395 A   | 17-10-1995       |
|  |                  | CA                      | 2186531 A1  | 05-10-1995       |
|  |                  | WO                      | 9526137 A1  | 05-10-1995       |
|  |                  | EP                      | 0752815 A1  | 15-01-1997       |
|  |                  | IL                      | 113070 A    | 28-10-1999       |
|  |                  | NZ                      | 283139 A    | 24-09-1998       |
|  |                  | ZA                      | 9502363 A   | 26-09-1995       |
| WO 9111105                             | A 08-08-1991     | CA                      | 2073768 A1  | 31-07-1992       |
|  |                  | AT                      | 110520 T    | 15-09-1994       |
|  |                  | AU                      | 642467 B2   | 21-10-1993       |
|  |                  | AU                      | 7210191 A   | 21-08-1991       |
|  |                  | BG                      | 96716 A     | 30-06-1994       |
|  |                  | DE                      | 69103745 D1 | 06-10-1994       |
|  |                  | WO                      | 9111105 A1  | 08-08-1991       |
|  |                  | EP                      | 0514417 A1  | 25-11-1992       |
|  |                  | ES                      | 2059117 T3  | 01-11-1994       |
|  |                  | IL                      | 97112 A     | 07-10-1994       |
|  |                  | JP                      | 2873084 B2  | 24-03-1999       |
|  |                  | JP                      | 5504567 T   | 15-07-1993       |
|  |                  | BG                      | 61246 B1    | 30-04-1997       |
|  |                  | BR                      | 9105930 A   | 10-11-1992       |
|  |                  | DK                      | 514417 T3   | 03-10-1994       |
|  |                  | FI                      | 923252 A    | 15-07-1992       |
|  |                  | IE                      | 910157 A1   | 14-08-1991       |
|  |                  | NO                      | 300352 B1   | 20-05-1997       |
|  |                  | NZ                      | 236990 A    | 25-02-1993       |
|  |                  | US                      | 5607681 A   | 04-03-1997       |
|  |                  | ZA                      | 9100763 A   | 26-02-1992       |
| DE 4301277                             | A 14-07-1994     | DE                      | 4301277 A1  | 14-07-1994       |